NEURAL SOURCE LOCALIZATION USING ADVANCED SENSOR ARRAY SIGNAL PROCESSING TECHNIQUES

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Abstract- **This paper aims to describe a hybrid technique that combines the feasibility of our recently developed *Multiresolution Analysis of Signal Subspace Invariance Technique* (MASSIT) [1] with the *Finite Element Method* (FEM) analytic model developed in [2] to obtain accurate localization scheme of neural sources in an extracellular recording environment. The power of the proposed method stems from the fact that robust array signal processing approach is fused with the FEM analysis yielding the closest scenario to practical experimental situations. Results from experimental signal and noise simulated composite are summarized and the overall performance is evaluated.**
Keywords **- Array processing, multichannel neural probes, source localization.**

I. INTRODUCTION

The need for accurate methods to determine neural source location relative to the recording micro-device in extracellular recording of neural activity in the brain becomes inevitable. Source localization helps to understand connectivity of small populations of neural cells and allows tracking of electrode motion without losing continuous recording of individual cells. Moreover, as cell localization schemes improve, controlled pharmaceutical delivery to sub-circuits of neural populations through special microprobe designs becomes more feasible.

Generally speaking, the amount of information to be revealed about neural cell location is very limited because of the tremendous challenges that face the implanted system. These range from the limited bandwidth of the telemetry system to the limited computational power that can be expected from the implant signal processor.

The main objective of this paper is to describe a hybrid signal processing scheme that integrates the information revealed by our recently developed *Multiresolution Analysis of Signal Subspace Invariance Technique* (MASSIT) for blind source identification described in [1,3] and the FEM analysis of neural tissue-microprobe interface environment summarized in [2]. Each of these techniques reveals different information that can be used to localize the neural source and they can be considered to complement each other. The integration of the overall information into a single array signal processor should be able to achieve the required goal of this work.

II. METHODOLOGY

Due to the nature of the neural signal with its well time-localized events or "spikes", the signal processing methodology should rely on time and frequency localization characteristics. These characteristics are strongly met by using the *Discrete Wavelet Transform* (DWT) as a front-end stage of MASSIT. The key feature in MASSIT is that it fuses the well developed techniques for multiresolution analysis of the signal with the well developed theory of array processing [4] in a unified framework. We briefly describe below the main approach of the technique but, for lack of space, we'll not attempt to provide mathematical details, which can be found in [1,5].

This section is subdivided in three parts. First, the key idea of MASSIT is described. Next, source separation is accomplished based on spatial filtering using signal subspace results from MASSIT. Finally, the approach for source localization is linked to the FEM results of [2]. The overall approach and preliminary results are summarized in the last section.

A. Multiresolution Analysis of Signal Subspace Invariance Technique (MASSIT)

The first step of the MASSIT involves performing a *Stationary Discrete Wavelet Packet Transformation* (SDWPT) [3] to the multichannel observation data matrix denoted $Y \in \Re^{MxN}$, where M denotes the number of channels, and N denotes the number of snapshots acquired by the array in time interval T. Assuming there are P neural sources impinging on the recording array, the classical model for Y is expressed as follows:

$$\boldsymbol{Y} = \boldsymbol{A}\,\boldsymbol{S} + \boldsymbol{Z} \tag{1}$$

where $A \in \Re^{MxP}$ denotes the mixing matrix, $S \in \Re^{PxN}$ denotes the signal matrix to be estimated, and $Z \in \Re^{MxN}$ denotes an *iid* additive noise component both spatially and temporally correlated. The technique doesn't assume any restriction on the cross correlation between the signal and noise, due to the strong background neural activity, which represents a major component of the observed noise process. This approach is the strongest and most realistic among all other array processing techniques [6] due to the nature of the neural signal environment. The obtained transformed multichannel coefficient matrix $Y_j \in \Re^{MxN}$ expresses Y in the wavelet domain in the j^{th} subband.

In a second step, the technique performs advanced signal processing computations involving *Singular Value Decomposition* (SVD) of the spatial covariance matrix $R_Y^j \in \Re^{MxM}$ of Y_j [7]. From a theoretic viewpoint, the information about the neural source's spatial amplitude distribution or "*footprint"* on the array side is contained in this covariance matrix. The SVD allows one to assess the P principal sources impinging on the array to obtain an estimate of the original source data matrix S at the array interface.

The third step in the algorithm estimates the mixing matrix A in each of the wavelet subbands from second order statistics or by estimating the signal and noise subspaces from the output

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Abstract

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of the SVD stage. The last step consists of selecting certain subbands from the full wavelet expansion that are guaranteed to span the signal subspace. The criterion by which a characteristic wavelet tree is selected for each source assumes that the signal subspace remains *invariant* across the multiresolution levels obtained in the wavelet domain. This is guaranteed to be true only in subbands where the corresponding wavelet basis functions span the signal's functional space. The separation of the P neural sources is achieved using a simple search in the wavelet decomposition tree to find nodes that best describe the signal energy based on three components describing the signal's energy distribution in space, time and scale domains. These are:

1- The eigenvalue distribution across tree nodes,
2- The characteristic tree shape.
3- The eigenvector describing the signal subspace.

Details of the algorithm can be found in [5]. Fig. 1 illustrates a schematic of the system.

It is worthy to mention that, due to the sparsity of the neural signal on the time base, a spike detection stage usually precedes the MASSIT stage so that the N snapshots of the array contain only a single event. It is likely that the length N time window may contain more than a single event belonging to different sources. In this latter case, the MASSIT automatically determines the number of sources P within N using a statistical Likelihood Ratio Test (LRT) and performs the appropriate separation [5,7]. This case is out of the scope of this paper. It will be henceforth assumed that the analysis described in the sequel is conducted for each detected event separately.

B. Spatial filtering for neural source separation

Once the mixing matrix A is obtained from MASSIT, it is feasible to obtain an estimate of the deterministic signal matrix S without estimating the noise correlation due of the compactness property of the transform that allows thresholding small coefficients, an operation often referred to as *denoising* [6]. Another way to estimate S can use the sparsity of the neural signal on the time base as stated earlier allowing the noise spatial covariance matrix $\boldsymbol{R}_Z \in \Re^{MxM}$ to be estimated from "*spike free*" data instants. Once this is achieved, the *minimum variance* BLUE (*Best Linear Unbiased Estimator* [7]) estimate of S can be obtained by using the signal subspace estimate from MASSIT. This is be expressed as

$$\widetilde{\boldsymbol{S}} = (\boldsymbol{A}^T \boldsymbol{R}_Z^{-1} \boldsymbol{A})^{-1} \boldsymbol{A}^T \boldsymbol{R}_Z^{-1} \boldsymbol{Y} \qquad (2)$$

The term that pre-multiplies the observation matrix $\boldsymbol{Y}$ is just the *Pseudo inverse* of the mixing matrix $\boldsymbol{A}$ that is used to cancel out all the interference and correlated noise components once the principal sources in $\boldsymbol{Y}$ are separated. If the noise covariance is diagonal (spatially uncorrelated), then this is equivalent to applying appropriate weights to every channel to maximize the SNR. If the noise is spatially colored, then the inverse of the noise covariance acts as a spatial filter for all non-principal components in $\boldsymbol{Y}$.

C. Localization of neural sources

The MASSIT relies on estimates of the signal subspace from data measurements and makes use of them to identify the best wavelet tree representing each source. The *array manifold*, defined as all the array responses, i.e. steering vectors obtained as the signal parameters vary over the entire parameter space can be obtained by modeling the array geometry using FEM in the extracellular tissue environment. The intersection of the estimated signal subspace for each neural source and the modeled array manifold will immediately enable the solution to the neural source localization problem in the absence of noise.

The study performed in [2] reveals some important results about how the array manifold can be modeled. By modeling the tissue media through which the signals pass from the source to the electrode array as a homogeneous resistive conductor with no space charge, the FEM solutions demonstrate the distortion of the electrical field lines by the presence of the non-conducting substrate of the array. The only good conductors are the recording sites at which the signal amplitude is estimated by the MASSIT stage and they are too small to distort the field further. Since it is assumed to have a poor interface to the tissue, the substrate interferes with the flow of current from a source to a sink surrounding the field of interest.

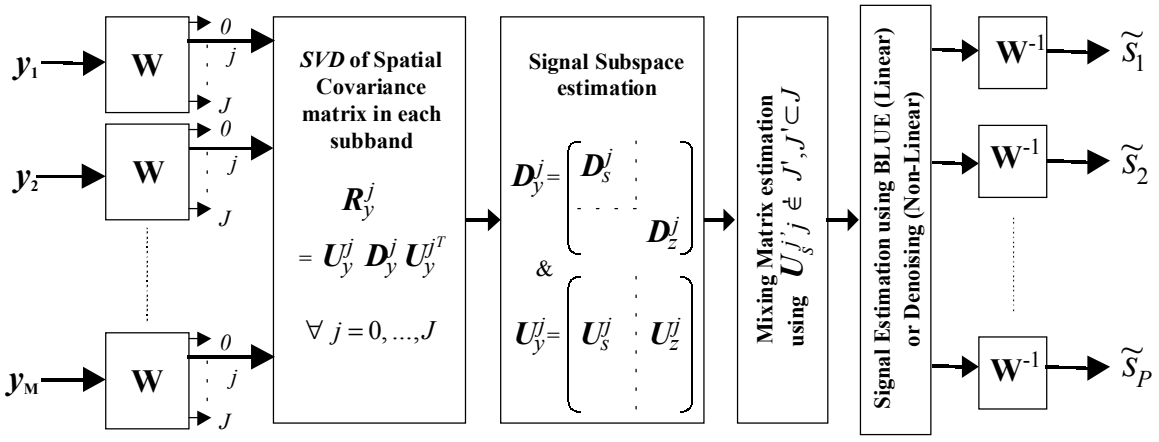

Fig. 1: Schematic of the MASSIT: The blocks $\mathbf{W}$, $\mathbf{W}^{-1}$ imply a SDWPT, and inverse SDWPT operators respectively. There are J+1 nodes in the wavelet packet tree (node *0* being the root level, i.e., the time domain signal, and $J = 2^{L+1}$-2, where L is the number of resolution levels, i.e., tree depth).

This phenomenon can be interpreted as an amplification of the observed signal particularly when the cell is directly over the substrate. Consequently, the signal's amplitude cannot be assumed to attenuate according to a simple 1/r or $1/r^2$ roll-off. This implies that there exists a point spread function for the source on the substrate that depends on the altitude and shift from the substrate center. In otherwords, the "*footprint*" of the cell on the array can be deconvolved to a point in space. Fig.(2) illustrates the point spread function hypothesis of the source relative to its position from the substrate center at different altitudes in two dimensional space.

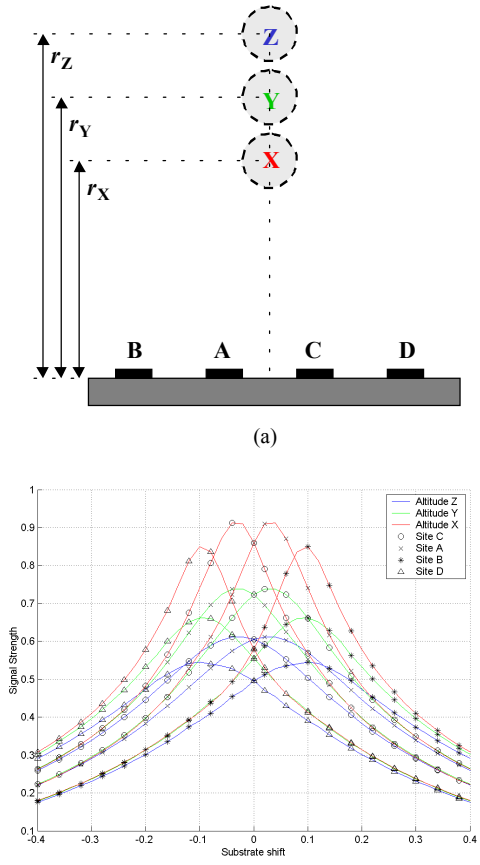

Fig. 2: (a) Approximate cell model in 3 different positions X, Y and Z above a 1D substrate with 4 sites. Altitudes above substrate are 0.05, 0.1 and 0.15 respectively. The substrate width is 0.2, and site spacing is 0.06. The origin is assumed at the substrate center. The source radius is 0.02 and the zero equipotential surface is at radius 1 from the origin. For clarity, the schematic is not to scale. (b) FEM solution for signal strength at X (red) , Y (green), and Z (blue) as function of the substrate shift from the origin.

The localization of the neural source is contingent upon estimating this point spread function and coupling it with the signal subspace estimated at the array.

The problem can thus be envisioned as two fold:

1- On the probe computational side, the spatial covariance matrix can be partitioned to subtract out common signal profiles of correlated sources, keeping only the independent uncorrelated part of each source to be localized.

2- On the brain side, the probe geometry is translated into gain functions that equalize the disturbance of the field at the recording sites.

By carefully examining the profiles in Fig.2-b, less skewness and higher peaks near the substrate center characterize low altitude sources. High altitude sources have broader, skewed and have lower peaks near the center. Since skewness is a function of the site position on the substrate, each probe geometry has an associated gain pattern that has to be included in the computations of the signal subspace to provide the localization information.

III. Results

The proposed method was implemented on a simulated data set extracted from experimental data. A total of $P = 4$ neural sources were detected across a subarray of 4 channels on a 2D array arranged as shown in Fig.3.

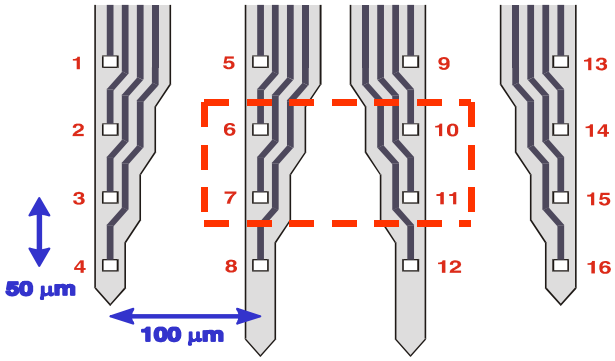

Fig. 3: 2D- 16 channel probe used for the data acquisition. Results for a subarray of channels 6,7, 10 and 11 were the neural activity is highest are shown in Fig. 4.

Template waveforms were obtained by averaging multiple realizations of these sources across time [8]. The spike waveforms are shown in Fig. 4 for each channel of the subarray. Experimental noise from spike-free data was extracted from the same subarray data.

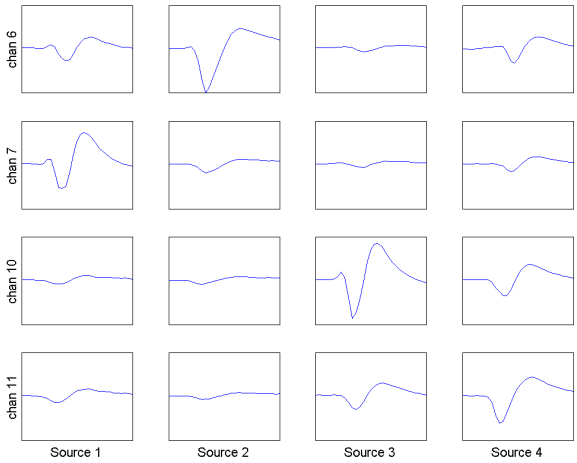

Fig.4.: Template waveforms for 4 neural sources detected across the subarray of channels 6, 7, 10 and 11 of Fig. 3.

For predetermined signal to noise ratios, the extracted noise was scaled and the template waveforms were added to the scaled noise at time intervals obtained from Poisson processes of known parameters. The simulation is thus the closest

scenario to a real experimental data set with the difference that event occurrence times were known before to the noise addition. This enabled to assess accurate performance of the technique under different SNRs. The simulated data set was processed with the MASSIT and the signal subspace estimate of each source is shown in Fig.5 for SNR = 12.5 dB.

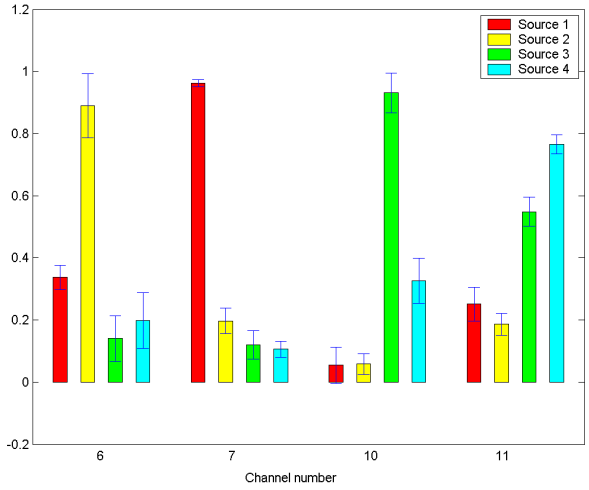

Fig. 5: MASSIT signal subspace estimates for SNR = 12.5 dB

The array manifold for the 2D probe geometry of Fig.3 can be obtained using a 3D FEM similar to the linear array illustrated in Fig.2-a. Studies are underway to integrate the FEM method in 3 dimensions with histological findings. The output is directly applied to the signal solution obtained from MASSIT to adjust for the substrate presence in the extracellular field. The parameter vector to be estimated consists of the shift, depth and altitude from the substrate center in the *x*, *y* and *z* directions, respectively. The array manifold for variable parameter vectors is calculated. Each parameter vector generated 4 profiles corresponding to the 4 sites similar to each altitude in Fig.2-b. The closest intersection, in a mean square sense, with the estimated signal subspace from MASSIT enables immediately to obtain the parameter vector describing the localization information from the assumed origin (substrate center).

VI. Conclusion

We have presented a new methodology for solving the localization problem of neural sources in extracellular recordings. The method relies on a two-stage process where estimates of the array response are derived from a robust array processing algorithm that estimates the neural source's *footprint* at the substrate. The neural signal is estimated using a linear unbiased estimator that has minimum variance. The next stage applies gain functions derived from FEM modeling of the substrate geometry to correct for the disturbance of the field caused by the presence of the nonconductive substrate. The outcome is used to estimate the neural cell location relative to the recording probe.

Current work is aimed to implement FEM models for each probe geometry and verify the consistency of the technique with different array manifolds. Meanwhile, histological methods involving staining techniques are being conducted in our lab to accurately determine the probe location after retract to verify the accuracy of the technique in locating sources in the proximity of the probe trace.

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